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**REMARKS**

Claims 1-61 and 109-119 are pending in the application. Claims 4-43, 45-50, 52, 55, 58, 61 and 109-119 are withdrawn from consideration and 1-3, 44, 51, 53, 56, 57, 59 and 60 are rejected.

Claims 1 and 57 have been amended and claims 2, 3, 44, 51 and 56 have been cancelled without prejudice or disclaimer. Accordingly, claims 1, 5-43, 45-50, 52-55, 57-61 and 109-119 will remain pending in the application upon entry of the instant amendment. Claim 1 has been amended to be commensurate in scope with claim 3 and claim 57 has been amended to depend from claim 1. Support for the amendments to claims 1 and 57 can be found throughout the specification and claims as originally filed. No new matter has been added.

Amendment and cancellation of the claims herein are not to be construed as an acquiescence to any of the rejections/objections made in the instant Office Action or in any previous Office Action, and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the claims as originally filed, or substantially similar claims, in one or more subsequent patent applications

***Claim Rejections - 35 U.S.C. §§102 and 103***

Claims 1-2, 44 and 56 are rejected under 35 U.S.C. §102 (a,b,e) as being anticipated by Pausch, *et al.* WO 95/21925. Applicants respectfully disagree and traverse the rejection.

However, without acquiescing to the rejection in any way and in order to expedite prosecution of the application, claims 2, 44 and 56 have been cancelled without prejudice or disclaimer, thereby obviating the rejection as to those claims. In addition, claim 1 has been amended to be commensurate in scope with claim 3. Inasmuch as claim 3 is not subject to the rejection, the rejection does not apply to claim 1 as amended herein. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1-2, 44 and 56 are rejected under 35 U.S.C. §102 (a,b,e) as being anticipated by Fowlkes, *et al.* WO 94/23025. Applicants respectfully disagree and traverse the rejection.

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However, without acquiescing to the rejection in any way and in order to expedite prosecution of the application, claims 2, 44 and 56 have been cancelled without prejudice or disclaimer, thereby obviating the rejection as to those claims. In addition, claim 1 has been amended to be commensurate in scope with claim 3. Inasmuch as claim 3 is not subject to the rejection, the rejection does not apply to claim 1 as amended herein. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1-2, 44, 56 and 57 are rejected under 35 U.S.C. §102 (e) as being anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Brown, *et al.* WO 99/214344. Applicants respectfully disagree and traverse the rejection.

However, without acquiescing to the rejection in any way and in order to expedite prosecution of the application, claims 2, 44 and 56 have been cancelled without prejudice or disclaimer, thereby obviating the rejection as to those claims. In addition, claim 1 has been amended to be commensurate in scope with claim 3, and claim 57 has been amended to depend from claim 1. Inasmuch as claim 3 is not subject to the rejection, the rejection does not apply to claim 1 as amended herein, or claim 57, which now depends from claim 1. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1-2, 44, 56 and 57 are rejected under 35 U.S.C. §103 (a) as being unpatentable over Pausch, *et al.* and Conklin, *et al.* Applicants respectfully disagree and traverse the rejection.

However, without acquiescing to the rejection in any way and in order to expedite prosecution of the application, claims 2, 44 and 56 have been cancelled without prejudice or disclaimer, thereby obviating the rejection as to those claims. In addition, claim 1 has been amended to be commensurate in scope with claim 3, and claim 57 has been amended to depend from claim 1. Inasmuch as claim 3 is not subject to the rejection, the rejection does not apply to claim 1 as amended herein, or claim 57, which now depends from claim 1. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1-2, 44, 56 and 57 are rejected under 35 U.S.C. §103 (a) as being unpatentable over Fowlkes, *et al.* WO94/23025. Applicants respectfully disagree and traverse the rejection.

However, without acquiescing to the rejection in any way and in order to expedite prosecution of the application, claims 2, 44 and 56 have been cancelled without prejudice or

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disclaimer, thereby obviating the rejection as to those claims. In addition, claim 1 has been amended to be commensurate in scope with claim 3, and claim 57 has been amended to depend from claim 1. Inasmuch as claim 3 is not subject to the rejection, the rejection does not apply to claim 1 as amended herein, or claim 57, which now depends from claim 1. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1-2, 44, 56 and 57 are rejected under 35 U.S.C. §103 (a) as being unpatentable over Brown, *et al.* WO99/14344 and Conklin, *et al.* Applicants respectfully disagree and traverse the rejection.

However, without acquiescing to the rejection in any way and in order to expedite prosecution of the application, claims 2, 44 and 56 have been cancelled without prejudice or disclaimer, thereby obviating the rejection as to those claims. In addition, claim 1 has been amended to be commensurate in scope with claim 3, and claim 57 has been amended to depend from claim 1. Inasmuch as claim 3 is not subject to the rejection, the rejection does not apply to claim 1 as amended herein, or claim 57, which now depends from claim 1. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 1-3, 44, 51, 53, 54, 56, 57, 59 and 60 are rejected under 35 U.S.C. §103 (a) as being unpatentable over Pausch, *et al.* WO95/21925. Fowlkes, *et al.* WO94/23025, Brown, *et al.* WO99/14344 and Conklin, *et al.* as applied to claims 1-2, 44, 56 and 57 above and further in view of Hamm. Applicants respectfully disagree and traverse the rejection.

However, without acquiescing to the rejection in any way and in order to expedite prosecution of the application, claims 2, 44, 51 and 56 have been cancelled without prejudice or disclaimer, thereby obviating the rejection as to those claims. In addition, claim 1 has been amended to be commensurate in scope with claim 3, and claim 57 has been amended to depend from claim 1. Applicants submit that claims 1, 53, 54, 57, 59 and 60 are patentable over the cited references, alone or in combination.

The Examiner admits that none of the primary references teaches or suggests additionally modifying the N-terminus portion of GPA-1 to operably link at least the first five N-terminal amino acids of a second heterologous G protein. However, the Examiner states that the Hamm reference teaches that in addition to the C-terminus of G protein alpha subunits being critical in determining receptor-G protein receptor specificity (as allegedly taught by the

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Pausch, Fowlkes, Brown and Conklin references), the N-terminus of the alpha G-protein subunit also *appears* to be involved in promoting heterologous receptor contact or coupling. [Emphasis added.] The Examiner concludes that Hamm provides the motivation to one of ordinary skill in the art to further modify the chimeric G alpha protein subunits obtained by Pausch, Fowlkes, Brown and Conklin by linking or substituting into the N-terminal portion of the reference chimeras corresponding heterologous amino acids in order to obtain sandwich chimeras that can be screened for different degrees of heterologous receptor coupling.

Applicants disagree. The Hamm reference does not teach or suggest linking or substituting into the N-terminal portion of the reference chimeras corresponding heterologous amino acids in order to obtain sandwich chimeras of the present invention. Contrary to the assertion of the Examiner, the Hamm reference does not teach that the N-terminus of G protein alpha subunits is critical to promoting heterologous receptor contact or coupling. In fact, there is nothing in Hamm that relates the structure and function of the N-terminus to the C-terminus such that one of ordinary skill in the art *should*, based on the teachings of Pausch, Fowlkes, Brown and Conklin, make similar linkings or substitutions in the N-terminus to obtain sufficient specificity to achieve functional coupling to the surrogate receptor.

In order to establish a *prima facie* showing of obviousness, the Examiner must show that the Hamm reference teaches that one of ordinary skill in the art *should* modify the teachings of the other references to arrive at the claimed invention, not that would could modify the teachings of the other references to arrive at the claimed invention. Even if Hamm does teach that the N-terminus of the alpha G-protein subunit *appears* to be involved in promoting heterologous receptor contact or coupling, such appearance is not enough to establish a *prima facie* showing of obviousness. At best, the Hamm reference teaches that it might be obvious to try to modify the N-terminus. However, obvious to try is not the test of obviousness. Unless the reference teaches that one should make the modification, it fails to render obvious the invention.

Moreover, there is no teaching in the Hamm reference, or any of the other references cited in the proposed combination, as to which amino acids in the N-terminus should be linked or substituted. Thus, even if there were motivation to combine the references, the combination does not put one of ordinary skill in the art in possession of all the elements of the claims at

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issue. Further more, even if Hamm does teach that the N-terminus of the alpha G-protein subunit *appears* to be involved in promoting heterologous receptor contact or coupling, such appearance is not enough to provide one of ordinary skill in the art with the requisite expectation of success in practicing the claimed invention.

In short, in the absence of the required motivation to combine and expectation of success, the instant rejection constitutes nothing more than a hindsight reconstruction of the invention based on Applicants' teachings. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

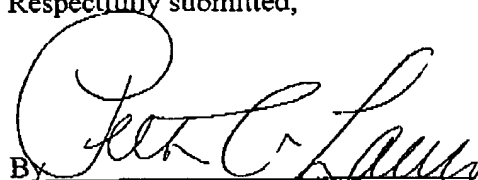
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**CONCLUSION**

In view of the foregoing, favorable reconsideration and withdrawal of all rejections and allowance of the application are respectfully solicited. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned attorney at (617) 439-4444.

Respectfully submitted,

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By 

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